(19) World Intellectual Property Organization International Bureau



(43) International Publication Date 3 May 2001 (03.05.2001)

PCT

(10) International Publication Number WO 01/30359 A1

- (51) International Patent Classification⁷: A61K 31/575. 31/718. 31/21, 35/78, A23L 1/30. A61P 3/06
- (21) International Application Number: PCT/SE00/02100
- (22) International Filing Date: 27 October 2000 (27.10.2000)
- (25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: 9903915-8

29 October 1999 (29.10.1999) S

- (71) Applicant (for all designated States except US): TRIPLE CROWN AB [SE/SE]; Björnnäsvägen 27, S-113 47 Stockholm (SE).
- (72) Inventor; and
- (75) Inventor/Applicant (for US only): SJÖBERG, Kjell [SE/SE]; Stenslingan 10, S-182 38 Danderyd (SE).
- (81) Designated States (national): AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES,

FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO. NZ, PL, PT, RO. RU. SD. SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

- With international search report.
- Before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments.

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

کر ہر

(54) Title: CHOLESTEROL LOWERING AND BLOOD LIPIDS LOWERING COMPOSITION

(57) Abstract: The present invention is a composition containing cholesterol lowering and blood lipids lowering components such as phytosterols in a biologically easily available form in combination with unsaturated fatty acids or esters, short chain fatty acids or esters and/or hydrolyzed flour containing β -glucan and amylodextrin; food containing such a composition and a method for manufacturing of such a composition.

Patent application no 9903915-8 Cholesterol lowering and blood lipids lowering composition. Priority date October 29,1999.

CHOLESTEROL LOWERING AND BLOODLIPIDS LOWERING COMPOSITION

BACKGROUND

Phytosterols such as β -sitosterol and β -sitostanol and their derivatives are used in medicine owing to their ability to lower total and LDL- cholesterol levels in blood.

Recent research has shown that n-3 polyunsaturated fatty acids present in fish oils such as eicosapentaenic acids (EPA) and docosahexaenic acids (DHA) positively effect our blood lipids (1). They are also building blocks in prostaglandins. Further a positive effect on blood lipids has been noted by intake of shorter fatty acids (2). Finally, the importance of a daily intake of β-glucan and amylodextrins is recommended by USDA. (3,4). These compounds can be recovered by hydrolysis of oat meal and can be made in gelform as hydrocolloids.

DESCRIPTION OF THE INVENTION

In the present invention is shown how sterols and/or stanols in a biologially easily available form has successfully been combined with other blood lipids lowering and cholesterol lowering compounds such as unsaturated fatty acids or their derivatives and/ or shorter fatty acids or derivatives of these and/or hydrolysed fibres containing β-glucan or amylodextrines. A clear

2

distinction between blood lipids lowering and cholesterol lowering action of these compound is not present, furthermore interactive effects may occur.

Sterols and/or stanols are initially mixed with an oil such as fish oil and esters of shorter fatty acids and glycerol. The mixture is transesterified in a known manner to mainly monoglycerides of fatty acids from fish oil or shorter fatty acids. In this way we obtain in only one process step an entirely new combination of cholesterol lowering sterols and or stanols and good fatty acids in a concentrate, in some cases in the same molecule. The concentrate can be used such, be tabletted, encapsulated or mixed with food. The concentrate can also be mixed with hydrolystid fibres in gel- or powder form. The obtained mixture contains all desired components for blood lipids lowering and cholesterol lowering effects. The obtained mixture can be mixed into food such as bread, cakes, flakes and other or be encapsulated or tabletted. The advantrages besides the pure biological are that the oxygene sensitive polyunsaturated fatty acids are stabilsed by the hydrolysed meal. The manufacturing process is simple and cheap. For different applications one or more of the components can be excluded. The present invention will be described below by non limiting examples.

EXAMPLE 1

55 g of fishoil, 25 g of short chain fatty acids, 18 g of glycerol and 40 g of sterols are mixed in a vessel under inert athmosphere and are transesterified at elevated temperatures in known way. After cooling to 50-80 °C the mixture is added to 400 g of a gel based on hydrolysed

meal under good stirring. If desired stabilisers for unsaturated fatty acids can be added and/or the mixture can be kept under inert athmosphere.

The obtained composition can be used as is or be mixed into various food.

EXAMPLE 2

50g of oil containing polyunsaturated fatty acids, 25 g of oils from short chain fatty acids, 18 g of glycerol and 40 g of sterols are mixed in a vessel under inert athmosphere and are transesterified at elevated temperatures in known way. After cooling to 50-80 °C the mixture is added to 2500 g of a gel based on hydrolysed oats fibre under good stirring.

The obtained composition can be used as is or be mixed into into various food.

EXAMPLE 3

55 g of an oil containing polyunsaturated fatty acids, 10 g of glycerol and 40 g of sterols are transesterified in known way as in example 1. After cooling to 50-80 °C the mixture is added to 400 g of a gel based on hydrolysed oats fibre under good stirring.

The obtained composition can be used as is or mixed into various food.

EXAMPLE 4

500 g of fish oil, 100 g of oil of short chain fatty acids, 150 g of glycerol and 300 g of sterols transesterified as in ex 1. The composition obtained can be used as such or mixed into different food, be encapsulated or tabletted.

L

EXAMPLE 5

of g of oils of short chain fatty acids, 18 g of glycerol and 40 g of sterols are mixed in a vessel under inert athmosphere and transesterified at elevated temperature in known way.

After cooling to 50-80 °C the mixture is added under good stirring to 400 g of gel based on hydrolysed oats fibre. The obtained composition can be used as is, be encapsulated, tabletted or mixed into different food.

EXAMPLE 6

40 g of sterols are dissolved in 50 g of fish oil and 40 g of a monoglyceride in a vessel under inert athmosphere at 100 °C. The composition obtained can be used as is, be encapsulated, tabletted or mixed into different food.

EXAMPLE 7

50 g of sterols are mixed with 65 g of oils of short chain fatty acids and 15 g of glycerol and the mixture is transesterified as in ex 1. The obtained composition can be used as is, be encapsulated, tabletted or mixed into different food.

EXAMPLE 8

20g of sterols are dissolved in 40g of monoglycerides at 85°C and added to 200g of gelbased hydrolysed oats fibre under good stirring. The composition obtained can be used as is, been capsulated, tabletted or mixed into various food.

CLAIMS

- 1. A composition containing cholesterol lowering and blood lipids lowering components in which phytosterols, mixed with esters of unsaturated fatty acids and/or esters of short chain fatty acids, are distributed in monomolecular, low associated or cluster form in hydrolysed fibres containing β-glucan and amylodextrines.
- A composition as in claim 1 in which the cholesterol lowering component contains
 β-sitosterol and/or β-sitostanol.
- A composition as in claim 1 in which the cholesterol lowering composition contains
 β-sitosteryl esters and/or β-sitostanyl esters of polyunsaturated fatty acids.
- A composition as in claim 1 in which the cholsterol lowering component contains
 β-sitosteryl esters and/or β-sitostanyl esters of short chain fatty acids.
- 5. A composition as in claim 1 in which the blood lipids lowering component contains fish oil and /or mono and diglycerides of polyunsaturated fatty acids.
- 6. A composition as in claim 1 in which the blood lipids lowering component contains triand/or mono- and diglycerides of short chain fatty acids.
- 7. A composition as in claim 1 in which the blood lipids lowering component contains a mixture of fish oil and triglycerides of short chain fatty acids.
- 8. A composition as in claim 1 in which the blood lipids lowering and stabilising component contains hydrolysed meal containing a soluble fibre such as β-glucan or amylodextrins.
- 9. Method to prepare a composition as in the claims 1-8 in which fish oil and/or triglycerides of short chain fatty acids are mixed with glycerol and phytosterols, transesterified at elevated temperatures at 130 230 °C and that the mixture obtained is spread and stabilised in a gel based on hydrolysed fibres.

6

- 10. Food containing a composition as in the claims 1-8 in a suitable amount for a cholesterol and blood lipids lowering effect.
- 11. Capsule or tablet containing a composition as in claims 1-8.

7

REFERENCES

- 1. Bartram, H.P.; Gostner, A. et al. Effect of dietary fish oil on fecal bile acid and neutral sterol excredon in healthy volunteers. Z. Ernaehrungsv.,iss. (1998), 37(Supl. 1),139-
- 2. Inglett, G.E.; Newman, R.K. Plant Foods Hum. Nutr. 1994, 45,53-61
- 3. Anderson, James W.; Smith, Belinda M.; Gustafson, Nansy J. Am. J. Clin. Nutr. 1994, 59(5, Suppi.), 1242-1247
- 4. Inglett, George E. Nutraceuticals: The key to healthier eating ChemTech. 1999, october, 38-42.

SUBSTITUTE SHEET (RULE 26)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/SE 00/02100

A. CLASSIFICATION OF SUBJECT MATTER

IPC7: A61K 31/575, A61K 31/718, A61K 31/21, A61K 35/78, A23L 1/30, A61P 3/06 According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: A61K, C11C, A23L, A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE, DK, FI, NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCU	MENTS CONSIDERED TO BE RELEVANT	
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Υ	WO 9925362 A1 (HENKEL KOMMANDITGESELLSCHAFT AUF AKTIEN), 27 May 1999 (27.05.99)	1-11
	·	
Y	CHEMTECH, October 1999, George E. Inglett: "Nutraceuticals: The Key to healthier eating. Grandma was right about eating your porridge. Three new fat substitutes provide safe and functional alternatives to fat additives in foods",page 38 - page 42	1-11
A	WO 9219640 A1 (RAISION MARGARIINI OY), 12 November 1992 (12.11.92)	1-11

Special categories of cited documents:		"T"	later document published after the international filing date or priority	
A	document defining the general state of the art which is not considered to be of particular relevance		date and not in conflict with the application but cited to understand the principle or theory underlying the invention	
"E"	carlier application or patent but published on or after the international filing date	~X~	document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive	
"L"	document which may throw doubts on priority claim(s) or which is		step when the document is taken alone	
	cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means		document of particular relevance: the claimed invention cannot be	
٠٥٠			considered to involve an inventive step when the document is combined with one or more other such documents, such combinate being obvious to a person skilled in the art	
"P"	document published prior to the international filing date but later than the priority date claimed	~&~	document member of the same patent family	
Date of the actual completion of the international search		Date o	if mailing of the international search report	
	· .		22 -02- 2001	
19	February 2001			
Name and mailing address of the ISA		Authorized officer		
	edish Patent Office	Ī		
Box	k 5055, S-102 42 STOCKHOLM	Anna	sjölund/EÖ	
Fac	simile No. +46 8 666 02 86	Telept	none No. + 46 8 782 25 00	

See patent family annex.

Form PCT ISA 210 (second sheet) (July 1998)

Further documents are listed in the continuation of Box C.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SF 00/02100

	PCT/SE	00/02100
C (Continu	nation). DOCUMENTS CONSIDERED TO BE RELEVANT	
Category*		es Relevant to claim No
A	WO 9915546 A1 (RAISIO BENECOL LTD.), 1 April 1999 (01.04.99)	1-11
A	STN International, File CA, Chemical Abstracts, volume 104, no. 19, 12 May 1986 (Columbus, Ohio, US), Asahi Denka Kogyo K. K.: "Health food containing unsaturated fatty acid glycerides and plant sterols"; & JP,A2,61015647, 19860123	1-11
A	Scandinavian Journal of Nutrition, Volume 44, 2000, Helena Gylling et al, "Plant sterols in nutrition page 155 - page 157	1-11
		
	,	
		·

Form PCT/ISA:210 (continuation of second sheet) (July 1998)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 00/02100

	document earch report		Publication date		Patent family member(s)	Publication date
WO	9925362	A1	27/05/99	AU	1560399 A	07/06/99
				DE	19750453 A	27/05/99
				EP	1028733 A	23/08/00
WO	9219640	A1	12/11/92	AU	664827 B	07/12/95
n O	52150.0	• • •	12, 12, 12	CA	2102112 A	04/11/92
	·			EP	0594612 A,B	04/05/94
				SE	0594612 T3	
				FI	98730 B,C	30/04/97
				FĪ	934869 A	03/11/93
				HK	1001951 A	00/00/00
	•			JP	6506909 T	04/08/94
				NO	304581 B	18/01/99
				NO	933966 A	02/11/93
				PL	166991 B	31/07/95
				DE	69127207 D,T	22/01/98
•	•			DK	594612 T	01/09/97
				FI	964951 A	11/12/96
				HU	65318 A	02/05/94
				HU	217625 B	28/03/00
				HU	9303111 D	00/00/00
	•			RU	2095367 C	10/11/97
				US	5502045 A	26/03/96
				US	5958913 A	28/09/99
WO	9915546	A1	01/04/99	AU	9164198 A	12/04/99
			• •	AU	9164298 A	12/04/99
				EP	1015476 A	05/07/00
				EP	1027368 A	16/08/00
				FI	973647 A	10/03/99
				FI	974563 A	29/04/99
	•			FI	974648 A	06/05/99
				WO .	9915547 A	01/04/99

Form PCT ISA 210 (patent family annex) (July 1998)

THIS PAGE BLANK (USPTO)